Figures 10 through 16. New Claims 34 through 63 have been added. New claims 34-63 recite specific features of rate controlling membranes for implantable drug delivery devices and methods for processing rate controlling membranes used in implantable drug delivery devices. Support for these amendments may be found, for example, at page 9, paragraph 00046; page 14, paragraph 00058; page 14, paragraph 00059; page 16, paragraph 00064; page 17, paragraph 00065; page 28, paragraph 00089 (Example 8); page 30, paragraph 00093 (Example 11); and Figures 10 through 16.

For completeness, enclosed with this Preliminary Amendment are 10 pages of marked up claims and 9 pages of clean claims.

Conclusions:

Entry of these preliminary amendments and early and favorable examination on the merits is hereby solicited.

Respectfully submitted,

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What is claimed is:

1. A rate controlling membrane for an implantable ~~controlled~~ drug delivery device characterized by being subjected to an elevated temperature of about 30° C to about 5° C below the melting temperature of the membrane polymer for a predetermined period of about 1 - 250 hours and subsequently incorporated into the delivery device.

~~2. A rate controlling membrane according to claim 1 wherein the membrane material is selected from the group consisting of ethylene vinyl acetate copolymers, polyethylene, ethylene copolymers, ethylene oxide copolymers, polyamides, cellulosic materials, polyurethanes, polyether blocked amides copolymers, and polyvinyl acetate.~~

3. A rate controlling membrane according to claim 1 wherein the membrane comprises polyurethanes or polyether blocked amides copolymers ~~ethylene vinyl acetate copolymer~~.

~~4. A rate controlling membrane according to claim 3 wherein the vinyl acetate content is about 4 - 18%.~~

~~5. A rate controlling membrane according to claim 4 wherein the membrane is characterized by a DSC profile having a primary peak at about 94 - 99°C and a secondary peak at greater than about 50° C.~~

~~6. A rate controlling membrane according to claim 5 wherein the vinyl acetate content is about 5 - 12%.~~

~~7. A rate controlling membrane according to claim 2 or 5 wherein the device is a transdermal drug delivery device comprising a drug reservoir layer between a backing layer and a contact adhesive layer, said rate controlling membrane is on the skin proximal side of the drug reservoir layer.~~

~~8. A rate controlling membrane according to claim 7 wherein the drug reservoir comprises a drug selected from the group consisting of testosterone, estradiol, and fentanyl~~.

~~9. A rate controlling membrane according to claim 2 or 5 wherein the device is a transdermal drug delivery device comprising a backing layer, a permeation enhancer reservoir containing a permeation enhancer on the skin proximal side of the backing layer, a drug reservoir layer containing at least one drug to be transdermally administered on the skin proximal side of the permeation enhancer reservoir, and a means for maintaining said drug device in drug transmitting relation with the skin, wherein the rate controlling membrane is positioned between the permeation enhancer reservoir and the drug reservoir.~~

10. A rate controlling membrane according to claim 3 ~~2~~ wherein the membrane comprises ~~a material selected from the group consisting of~~ polyurethanes ~~or polyether blocked amides copolymers.~~

11. A rate controlling membrane according to claim ~~10~~ 1wherein the membrane is positioned in sealing relationship with an internal surface of one end of an impermeable reservoir of a fluid-imbibing drug delivery device, wherein said fluid imbibing drug delivery device comprises an impermeable reservoir containing a piston that divides the reservoir into a drug containing chamber and a water-swellable agent containing chamber, wherein the water-swellable agent containing chamber is provided with an outlet which accommodates said membrane.

12. A rate controlling membrane according to claim ~~11~~ 3 wherein the drug containing chamber comprises leuprolide.

13. A rate controlling membrane according to claim 1 wherein the elevated temperature is about 45 - 80° C and the predetermined period is about 1-75 hours.

14. A rate controlling membrane ~~according to claim 1~~ for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 30° C to about 5° C below the melting temperature of the membrane polymer for a predetermined period of about 1 to 250 hours and

subsequently incorporated into the delivery device wherein the membrane is cooled to ambient conditions before being incorporated into the delivery device.

15. A rate controlling membrane according to claim 3 wherein the elevated temperature is about 52 - 72° C and the predetermined time is about 2 - 36 hours.

16. A rate controlling membrane according to claim 10 wherein the elevated temperature is about 55 - 75° C and the predetermined time is about 12 - 48 hours.

17. A method for processing rate controlling membranes used in ~~controlled~~ implantable drug delivery devices comprising:

a) allowing the membrane to relax at room temperature for about 12 hours to 7 days before being subjected to elevated temperature;

~~a~~b) exposing the membrane to a predetermined temperature of from about 30° C to about 5°C below the melting temperature of the membrane polymer;

~~b~~c) maintaining the membrane at the predetermined temperature for a period of time of from about 1 to 250 hours; and

~~c~~d) incorporating said membrane into a controlled drug delivery device.

18. A method according to claim 17 wherein the predetermined temperature is from about 45° C to 80° C.

19. A method according to claim 18 wherein the membrane is maintained at the predetermined temperature for a period of time of from about 1 to 75 hours.

20. A method according to claim 17 wherein the membrane is cooled to ambient conditions over a period of time of about 0.1-150 hours prior to incorporating the membrane into the device.

~~21. A method according to claim 17 wherein the membrane is incorporated into a transdermal drug delivery device and comprises an increased drug permeability compared to a non-annealed membrane of the same materials.~~

22. A method according to claim 17 wherein the membrane is formed from a material selected from the group consisting of ~~ethylene vinyl acetate copolymers, polyethylene, ethylene copolymers, ethylene oxide copolymers, polyamides, cellulosic materials,~~ polyurethanes, and polyether blocked amides copolymers, ~~and polyvinyl acetate~~.

~~23. A method according to claim 17 wherein the membrane is formed from ethylene vinyl acetate copolymer.~~

~~24. A method according to claim 23 wherein the membrane comprises 4-18% vinyl acetate.~~

~~25. A method according to claim 24 wherein the membrane comprises 5-12% vinyl acetate.~~

~~26. A method according to claim 24 wherein the predetermined temperature is about 52 - 72° C and the period of time is about 2 - 36 hours.~~

~~27. A method according to claim 17 wherein the membrane is formed from high density polyethylene.~~

28. A method according to claim 17 wherein the membrane is allowed to set at ambient conditions for a period of at least about 12 hours after processing prior to exposing the membrane to said predetermined temperature.

29. A method according to claim 28 wherein the membrane is allowed to set at ambient conditions for a period of at least 48 hours after processing prior to exposing the membrane to said predetermined temperature.

30. A method according to claim 17 wherein the membrane comprises polyurethane.

31. A method according to claim 30 wherein the predetermined temperature is about 55 - 75° C and the period of time is about 12 - 48 hours.

32. A method according to claim 31 wherein the membrane is positioned in sealing relationship with an internal surface of one end of an impermeable reservoir of a fluid-imbibing drug delivery device, wherein said fluid imbibing drug delivery device comprises an impermeable reservoir containing a piston that divides the reservoir into an active agent containing chamber and a water-swellable agent containing chamber, wherein the water-swellable agent containing chamber is provided with an outlet which accommodates said membrane.

33. A method according to claim 32 wherein the membrane is plug-shaped.

34. A rate controlling membrane according to claim 1 wherein the membrane comprises polyether blocked amides copolymers.

35. A rate controlling membrane according to claim 10 wherein the polyurethane is a single aliphatic polyether polyurethane or a blend of aliphatic polyether polyurethanes.

36. A rate controlling membrane according to claim 11 wherein the drug containing chamber comprises an opioid analgesic drug.

37. A rate controlling membrane according to claim 11 wherein the drug containing chamber comprises an antiviral drug.

38. A rate controlling membrane according to claim 11 wherein the drug containing chamber comprises an antineoplastic drug.

39. A rate controlling membrane according to claim 10 wherein the membrane is allowed to relax at room temperature for about 12 hours to 7 days before being annealed.

40. A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 30° C to about 5° C below the melting temperature of the membrane polymer for a predetermined period of about 1 to 250 hours and subsequently incorporated into

the delivery device wherein the membrane is allowed to relax at room temperature for about 12 hours to 7 days before being annealed.

41 A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 52° C to about 72° C for a predetermined period of about 2 to 36 hours and subsequently incorporated into the delivery device.

42. A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 52° C to about 72° C for a predetermined period of about 2 to 36 hours and subsequently incorporated into the delivery device wherein the membrane is cooled to ambient conditions before being incorporated into the delivery device.

43. A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 52° C to about 72° C for a predetermined period of about 2 to 36 hours and subsequently incorporated into the delivery device, wherein the membrane is allowed to relax at room temperature for about 12 hours to 7 days before being subjected to an elevated temperature.

44. A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 52° C to about 72° C for a predetermined period of about 2 to 36 hours and subsequently incorporated into the delivery device wherein during processing the membrane is dried to about 0 to about 1 % moisture content before being annealed and wherein the membrane is kept at about 0 to about 1% moisture content during annealing.

45. A rate controlling membrane for an implantable drug delivery device characterized by allowing the membrane to relax at room temperature for about 12 hours to 7 days before being annealed; subjecting the membrane to an elevated temperature of about 52° C to about 72° C for a predetermined period of

about 2 to 36 hours; and cooling the membrane to ambient conditions before being incorporated into the delivery device.

46. A rate controlling membrane for an implantable drug delivery device characterized by allowing the membrane to relax at room temperature for about 12 hours to 7 days before being annealed; drying the membrane to about 1 to 2% moisture content; subjecting the membrane to an elevated temperature of about 52° C to about 72° C for a predetermined period of about 2 to 36 hours while keeping the moisture content of the membrane at about 1 to 2%; and cooling the membrane to ambient conditions before being incorporated into the delivery device.

47. A rate controlling membrane according to claim 10 wherein the elevated temperature is about 50 - 80° C and the predetermined time is about 4 hours – 72 hours.

48. A method for processing rate controlling membranes used in implantable drug delivery devices comprising:

a) allowing the membrane to relax at room temperature for about 12 hours to 7 days;

b) exposing the relaxed membrane to a predetermined temperature of from about 30° C to about 5°C below the melting temperature of the membrane polymer;

c) maintaining the membrane at the predetermined temperature for a period of time of from about 1 to 250 hours; and

d) incorporating said membrane into a controlled drug delivery device.

49. A method for processing rate controlling membranes used in implantable drug delivery devices comprising:

a) allowing the membrane to relax at room temperature for about 12 hours – 7 days;

b) exposing the relaxed membrane to a predetermined temperature of from about 30° C to about 5°C below the melting temperature of the membrane polymer;

c) maintaining the membrane at the predetermined temperature for a period of time of from about 1 to 250 hours;

d) allowing the annealed membrane to cool to room temperature for about 0.1 to 250 hours; and

e) incorporating said membrane into a controlled drug delivery device.

50. A method according to claim 17 wherein the membrane comprises polyether blocked amides copolymers.

51 A method according to claim 50 wherein the predetermined temperature is about 55-75° C and the period of time is about 12 – 48 hours.

52 A method according to claim 51 wherein the membrane is positioned in sealing relationship with an internal surface of one end of an impermeable reservoir of a fluid-imbibing drug delivery device, wherein said fluid imbibing drug delivery device comprises an impermeable reservoir containing a piston that divides the reservoir into an active agent containing chamber and a water-swellable agent containing chamber, wherein the water-swellable agent containing chamber is provided with an outlet which accommodates said membrane.

53. A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 45° C to about 80° C for a predetermined period of about 1 – 75 hours and subsequently incorporated into the delivery device.

54. A method for processing rate controlling membranes with low variability of water uptake from membrane to membrane for an implantable drug delivery device comprising:

a) allowing the membrane to relax at room temperature for about 12 hours – 7 days;

b) drying the moisture content of the membrane to about 0 to about 1%;

c) exposing the relaxed membrane to a predetermined temperature of from about 30° C to about 5°C below the melting temperature of the membrane polymer while maintaining the low moisture content of the membrane;

d) maintaining the membrane at the predetermined temperature for a period of time of from about 1 to 250 hours;

e) allowing the annealed membrane to cool to room temperature for about 0.1 to 250 hours; and

f) incorporating said membrane into a controlled drug delivery device.

55. A rate controlling membrane for an implantable drug delivery device with decreased variability of water uptake from membrane to membrane.

56. A rate controlling membrane for an implantable drug delivery device characterized by being subjected to an elevated temperature of about 55° C - 75° C for a predetermined period of about 12 – 48 hours wherein the membrane comprises a material selected from the group consisting of polyurethanes or polyether blocked amides copolymers.

57. A method for processing rate controlling membranes used in implantable drug delivery devices comprising:

a) allowing the membrane to relax at room temperature for about 12 hours to 7 days before being subjected to elevated temperature;

b) exposing the membrane to a predetermined temperature of from about 45° C to about 80°C;

c) maintaining the membrane at the predetermined temperature for a period of time of from about 1 to 250 hours; and

d) incorporating said membrane into a controlled drug delivery device.

58. A method for processing rate controlling membranes used in implantable drug delivery devices comprising:

a) allowing the membrane to relax at room temperature for about 12 hours to 7 days before being subjected to elevated temperature;

a) exposing the membrane to a predetermined temperature of from about 45° C to about 80°C;

b) maintaining the membrane at the predetermined temperature for a period of time of from about 1 to 75 hours; and

c) incorporating said membrane into a controlled drug delivery device.

59. A rate controlling membrane according to claim 3 wherein the membrane comprises polyether blocked amides copolymers.

60. An annealed rate controlling membrane for an implantable drug delivery device wherein the annealed membrane exhibits more stable water uptake and more stable water permeability than a non-annealed membrane.

61. An annealed rate controlling membrane for an implantable drug delivery device wherein the annealing process decreases the variability of water uptake from membrane to membrane over time.

62. A rate controlling membrane according to claim 1 wherein the drug containing chamber comprises leuprolide.

63. A rate controlling membrane according to claim 10 wherein the drug containing chamber comprises leuprolide.